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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/606,779	06/28/2000	John H. Griffin	SCRIP1180-3	1406

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EXAMINER	
SAUNDERS, DAVID A	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 03/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
606,779	GRIFFIN et al
Examiner	**Group Art Unit**
SAUNDERS	1644

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☑ Responsive to communication(s) filed on 9/5/03.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☑ Claim(s) 2-22 is/are pending in the application.

Of the above claim(s)____ is/are withdrawn from consideration.

☐ Claim(s)____ is/are allowed.

☑ Claim(s) 2-22 is/are rejected.

☐ Claim(s)____ is/are objected to.

☐ Claim(s)____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number)____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received:____.

Attachment(s)

☑ Information Disclosure Statement(s), PTO-1449, Paper No(s).____

☐ Interview Summary, PTO-413

☑ Notice of Reference(s) Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Other____

Office Action Summary

Claims 2-22 are pending. Claims 2-22 are under examination.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/5/03 has been entered.

112 considerations are presented infra.

Claim 16 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 16 is confusing by reciting "the anticoagulant is heparin". Base claim 2 requires that the anticoagulant be an oral anticoagulant, but heparin is not an anticoagulant that is administered orally; heparin is administered by injection (PDR, pg 2538, col. 2).

Claim 22 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 20 and 22 recite new matter.

In claim 20 "the mutation occurs at position 506 of Factor V" recites new matter. This is a new subgenus of mutations because the only disclosed mutation at position 506 is that of Arg to Glu.

Regarding claim 22, the examiner finds no teaching of "anticoagulant neutralization" anywhere in the original disclosure. Applicant cannot introduce a negative limitation regarding a feature that was not disclosed. Ex parte Grasselli 231 USPQ 393. Further, Example 4 cannot support as applicant urges, because the exemplification of a test with added heparin is not an exemplification of a test with an oral anticoagulant (see 112, 2nd supra).

Prior art considerations are set forth infra.

Claims 2-22 are rejected under 35 U.S.C. 102(a) as being anticipated by Sun et al, for reasons of record in papers 14 and 18.

Applicant has urged that claim 2 and its dependents are not anticipated because the teachings regarding patients on oral anticoagulant or heparin therapy, at page 3124, col. 1, are merely suggestions and that one would need to confirm these by actual experiments, as in the instant disclosure. This argument is unconvincing because applicant has offered no objective reasons as to why one would have expected that what Sun et al teach would involve unpredictable experimentation. Further, the examiner considers notes that MPEP 2123 cites numerous decisions that hold a cited reference need not exemplify all that it teaches. While these decisions relate to patent references, the examiner deems that this principle applies all the more to reviewed journal publications, because authors thereof are reluctant to risk their professional reputations by making puffed up claims about the applicability of their discoveries.

In addition, the examiner does not consider that instant Example 4 makes up for the alleged deficiency in the disclosure of Sun et al. Example 4 pertains to samples spiked with heparin, which is not an oral anticoagulant (112 supra) as required by base claim 2. If applicant wants to argue that the effects of heparin upon the test would be unpredictable, he must like wise

argue that the effects of another anticoagulant, such as the oral anticoagulant Warfarin, upon the test would be unpredictable. Note that heparin and Warfarin act by different mechanisms in their anticoagulant activities (PDR at pages 694 and 2538). Thus instant Example 4 has done nothing to demonstrate that the test disclosed by Sun et al can be used for samples from patients on oral anticoagulant therapy. However, the examiner wants to make it clear on the record that he does not consider the results of testing with samples from patients treated with Warfarin to be unpredictable; note that Warfarin (Coumadin) acts by suppressing the synthesis of vitamin K dependent coagulation factors (PDR, pg 694, col. 1); thus one of skill would have reasonably expected that the Factor V deficient plasma, provided for dilution of the sample as taught by Sun et al, would serve to introduce all Factors, but factor V, including those Factors whose synthesis is suppressed by Warfarin.

Regarding claim 16, which is inconsistent with base claim 2, this is rejected, because Sun et al do mention patients treated with heparin at page 3124, col. 1 and because the examiner does not consider their teachings as pertaining to unpredictable embodiments.

New claim 17 is included in the rejection, despite applicant's urgings that Sun et al do not run their test reactions in parallel, with and without APC. To the contrary, the examiner finds that Sun et al did obtain several results by running assay samples in parallel, with and without APC. Note page 3120, col. 2, para. headed "Clotting Assays", line 8 thereof. Note also page 3122, para. spanning cols. 1-2 and Fig 3; note therein the teaching of "the prolongation of the APTT produced by APC"; any such "prolongation" can only be observed if there is an test sample without APC, against which the sample with APC can be compared.. Note also page 3123, col. 1 and Fig. 5.

From the considerations set forth supra regarding the recitation of "oral anticoagulant regimen" in claim 2 and "no APC is added" in claim 17, the examiner has included instant 18 and its dependents..

New claim 22 is rejected because Sun et al mention nothing about an anticoagulant neutralization step.

Applicant's arguments filed 9/5/03 have been fully considered but they are not persuasive for reasons noted above.

The Dahlback/Dahlback et al references of record are considered infra.

The examiner considers that claim 2 and its dependents are not anticipated by Dahlback (WO 94/17415) and Dahlback et al (PNAS 1994). From Dahlback's disclosure at page 21, last para. the examiner calculates Dahlback's calcium concentration to be, after dilution into the reaction mixture, approx. 1 mM. Likewise, the examiner calculates Dahlback's APC concentration, after dilution into the reaction mixture, to be approx. 39 ng/ml; this calculation assumes the m.w. of APC is approx. 61,000 (see US Pat. 5,198,534 at col. 1, lines 5-31 for m.w. of APC). These concentrations are not within the ranges recited in instant claim 2. Other than what Dahlback discloses at page 21, the teachings set forth no concentrations of calcium and APC in a coagulation assay.

Claims 18-19 are rejected under 35 U.S.C. 103(a) as being obvious over Dahlback (WO 94//17415) in view of The Merck Manual and the PDR.

Dahlback anticipates claim 18 because he teaches a like assay, in which there is a dilution of a sample into Factor V-deficient plasma (page 21). He also runs each sample in parallel without addition of APC. As to the limitation in claim 18, that the patient be on an "oral

anticoagulant regimen", Dahlback does not literally refer to patients on an "oral anticoagulant regimen"; however, he does refer to assaying samples from patients "on treatment with vitamin K antagonists" (page 17, line 10), and he teaches what factors can be added to compensate for deficiencies of Factors in such samples; "comprising" language of instant claims opens the scope to include such additions. Since Warfarin is an old and well known anticoagulant (Merck Index, pg 9954) and acts by suppressing the synthesis of Vitamin K dependent coagulation factors (PDR, pg 894, col. 1), it is taken that one of ordinary skill would have realized that the teachings of Dahlback at page 17 are applicable to assaying samples from patients on Warfarin, which is an "oral anticoagulant".

Regarding dependent claim(s) 19, note Dahlback teaches a mutation of Factor V at page 20. Therein he doe not mention whether the defect results from a homozygous or heterozygous condition. However, for a mutation in any gene, there will be individuals heterozygous and individuals homozygous for the mutation. If the mutation results in a pathological condition, individuals who are homozygous for the mutation will certainly exhibit the pathological condition, irrespective of whether the effect of the mutation is dominant or recessive. Thus anyone with a minimal knowledge of genetics would have been led to consider testing for a patient whose disorder is associated with a homozygous mutation in Factor V.

Dahlback et al (PNAS, 1994) are not cited; they teach nothing about assaying samples from patients being treated with Vitamin K antagonists.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A Saunders, PhD whose telephone number is 571-272-0849.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Typed 3/6/04 DAS

David A. Saunders

DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT ~~182~~ 1644